

REMARKS

Status of the Claims.

Claims 1-21 are pending with entry of this amendment, no claims being cancelled and no claims being added herein. Claims 1, 7, and 8 are amended herein. These amendments introduce no new matter. The amendment to claims 7 and 8 simply corrects a typographical error. The amendment to claim 1 is for clarity and finds support in the claim as filed and throughout the specification (e.g., page 2, lines 26-28, page 3, lines 12-15, page 3, lines 15-17, and so forth). It is noted that "a binding partner for each of two or more analytes" would require two or more binding partners. For purposes of clarity this is made express in claim 1. It is noted that the amendments made herein, do not alter the scope of the claimed invention and are made for clarity not for purposes of patentability.

Objection to the Specification.

The disclosure was objected to because the first paragraph did not recite the U.S. Patent Number for Application Number 09/358,204. The specification has been amended herein to insert the referenced patent number thereby obviating this objection.

Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statement (Form 1449) submitted on June 4, 2001.

Claim Objections.

Claim 7 and 8 were objected to because the allegedly appeared to be missing the word "surface" at the end of the claim. Claims 7 and 8 are amended herein to insert the word "surface" thereby obviating this objection.

35 U.S.C. §102.

Claims 1, 3-8, and 10-18 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Anderson *et al.* (U.S. Patent No: 6,168,948 B1). Applicants traverse.

The Examiner is respectfully reminded that anticipation requires that "all limitations of the claim are found in the reference, or 'fully met' by it." [emphasis added] *Kalman v Kimberly-Clark Corp.*, 218 USPQ 781, 789 (Fed. Cir. 1983).

In the instant case, claim 1, as amended herein recites:

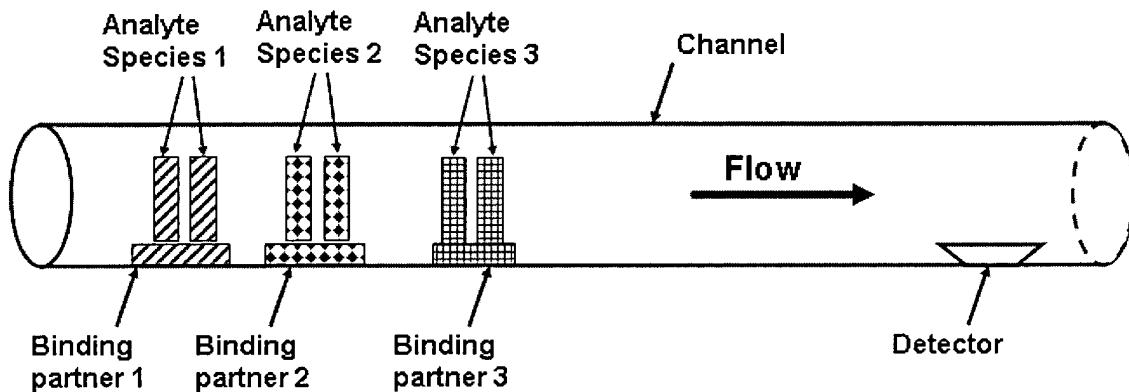
1. (Currently Amended) A method of detecting two or more target analytes in a sample, said method comprising:

i) providing a channel having affixed therein two or more binding partners each specific for one of said two or more analytes, where the binding partners for each of said two or more analytes are located in different regions of said channel and said channel has a cross-sectional area small enough such that when analytes are released from said two or more binding partners into a fluid flowing through said channel, said analytes remain spatially segregated until they reach a detection point in said channel downstream from said binding partners; . . .

Moreover, as explained in the specification:

In one preferred embodiment, this invention comprises a channel having attached therein binding partner(s) specific for the analytes that it is desired to detect. Different binding partners are located in different regions of the channel so that when the analyte(s) are bound they are "spatially encoded" by their location along the channel. The bound analytes are subsequently released from the binding partner, or the binding partner/analyte complex is released from the wall of the channel, into a fluid flowing through the channel. The channel dimensions are such that the analytes remain spatially segregated until they reach a detection point in the channel downstream from said binding partners.

An embodiment of this invention showing multiple analytes (analyte species 1, 2, and 3) is illustrated schematically below:



Anderson *et al.* fails to disclose or to even suggest a device comprising providing a channel having affixed therein two or more binding partners each specific for one of said two or

more analytes, where the binding partners for each of said two or more analytes are located in different regions of said channel.

In contrast, the device disclosed by Anderson *et al.* contains at most a single species of binding partner and is incapable of spatially segregating analytes along a channel as is accomplished in the presently claimed device. Thus, for Example, the embodiment identified by the Examiner contains only a single species of binding partner (a poly-T oligonucleotide):

In another embodiment of the present invention, a miniaturized m-RNA purification system and method are disclosed. Since messenger RNA comprises only a small fraction (e.g., about 20%) of the total cell RNA, it would be desirable to purify m-RNA from messenger expression monitoring applications. Messenger RNA can be distinguished by its poly-A tail. In this device, poly-T oligos are tethered on a high surface geometry. The messenger RNA will selectively hybridize to these oligonucleotides.

Referring to FIG. 27, a messenger RNA purification system 2900 includes a sheet 2902, such as polycarbonate, glass, silicon, or polypropelene, polystyrene, polyethylene, acrylic, and commercial polymers, and a substrate 2904 (e.g., silicon) having a plurality of ridges 2906 between the sheet 2902 and substrate 2904. Preferably, sheet 2902 is a polymer and substrate 2904 is silicon, but such composition is not limiting as other workable compositions are equally possible. The ridges 2906 are preferably formed using reactive ion etching or other conventional techniques. Poly T oligos or other affinity treatment 2912 are attached to ridges 2906, as discussed below. A piezoelectric crystal 2908 is preferably mounted to the polymeric sheet 2902 opposite substrate 2904. [emphasis added] (col. 41, lines 22-44)

This embodiment comprises only a single species of binding partner; poly-T oligos (oligonucleotides). Moreover, that single species of binding partner appears to be distributed throughout the reaction chamber (*see, e.g.*, 2912 in Figure 27 and accompanying explanation).

All species of mRNAs in the sample will bind to the poly-T oligos by virtue of their complementary poly-A tails. Because there is only a single species of binding partner (poly-T oligos), and all the mRNAs have poly-A tails, hybridization will result in the distribution of various mRNAs throughout the chamber 2910. **No spatial segregation of different analytes (different mRNAs) can occur.**

Even if the Examiner regards the mRNA as a first analyte, and the remaining RNA as a second analyte, the device disclosed by Anderson *et al.* fails to anticipate the presently

pending claims. Anderson *et al.* discloses only a single binding partner (poly-T oligos). There is no binding partner for the RNA that is not mRNA.

In summary, Anderson *et al.* :

- 1) Fails to disclose a device comprising a channel having affixed therein two or more binding partners each specific for one of said two or more analytes; and
- 2) Fails to disclose a device where binding partners for each of said two or more analytes are located in different regions of said channel.

Moreover, as explained above, because the Anderson *et al.* device comprises only a single binding partner (poly-T oligo) the device does not permit the detection of two or more target analytes. Consequently Anderson *et al.* a device or a method incorporating all the limitations of the presently claimed method. Accordingly, Anderson *et al.* fails to anticipate presently pending independent claim 1 or dependent claims 3-8, and 10-18 and the rejection of these claims under 35 U.S.C. §102(b) should be withdrawn.

If the Examiner wishes to maintain this rejection, Applicants request that she specifically identify all of the elements of claim 1 in the reference. In particular, Applicants request that she identify two or more binding partners each specific for one of said two or more analytes, where the binding partners for each of said two or more analytes are located in different regions of a channel.

35 U.S.C. §103(a).

Claims 2, and 19-21 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Anderson *et al.* (U.S. Patent No: 6,168,948). Claim 9 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Anderson *et al. supra*, in view of Yager (U.S. Patent No: 6,007,775). The Examiner alleged that Anderson *et al.*, at col. 41, lines 31-58, teaches a method of detecting two or more analytes in a sample using a channel having affixed therein a binding partner for each of the two or more analytes where the binding partners are located in different regions of the channel. The Examiner further alleges that because Anderson *et al.*, that the recitation at col. 11, lines 20-21, that the analytes are "generally be labeled" suggests that the analytes are sometimes not labeled and argues that

it would be obvious to sue the unlabeled analytes in the method of Anderson *et al.* With respect to claim 21, the Examiner argues it would be obvious using routine experimentation to amplify the analytes whereby analytes having an original concentration of less than 10-9 are detected. With respect to claim 9, the Examiner cites Yager as allegedly teaching the use of low Reynold's number channels. Applicants traverse.

A *prima facie* case of obviousness requires that the combination of the cited art, taken with general knowledge in the field, must provide all of the elements of the claimed invention. When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Moreover, to support an obviousness rejection, the cited references must additionally provide a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), *citing In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

The combination of the cited references fails to teach or suggest the presently claimed invention. As explained above, the presently claimed methods involve:

- i) providing a channel having affixed therein two or more binding partners each specific for one of said two or more analytes, where the binding partners for each of said two or more analytes are located in different regions of said channel and said channel has a cross-sectional area small enough such that when analytes are released from said two or more binding partners into a fluid flowing through said channel, said analytes remain spatially segregated until they reach a detection point in said channel downstream from said binding partners; . . . [emphasis added] (claim 1)

Anderson *et al.* at most teaches the use of a reaction chamber **2910** comprising a single binding partner **2912** (poly-T oligos). This reference fails to teach the detection of multiple analytes or to teach or suggest a device comprising a channel having two or more binding partners. Accordingly, Anderson *et al.* fails to render the pending claims obvious.

The defects of Anderson *et al.* are not remedied by Yager. Yager describes a microfabricated sensor that produces a sample stream and a carrier stream that flow in layers, one on top of the other. Reagents (indicator molecules) are introduced into the carrier stream while a sample is introduced into the sample stream. As the reagents and sample diffuse together they produce a detectable signal.

The reagent and the sample interact in a fluid phase, neither reagent nor sample are immobilized. The sensors described by Yager thus do not utilize a " providing a channel having affixed therein two or more binding partners each specific for one of said two or more analytes ". Indeed, the Examiner only cites Yager as allegedly teaching a channel having a Reynolds number below about 1.

Yager thus fails to remedy the deficiencies of Anderson *et al.*, and the combination of these references fails to provide the presently claimed invention. Accordingly, the Examiner has failed to make his *prima facie* case, and the rejection of claims 2, and 19-21 under 35 U.S.C. §103(a) should be withdrawn.

Obviousness-Type Double Patenting.

Claims 1-18 were rejected under the judicially created doctrine of obviousness-type double patenting in light of claims 15-46 of U.S. Patent 6,361,671. Applicants respectfully traverse.

Contrary to the Examiner's assertion claims 15-46 of U.S. Patent 6,361,671 fail to teach or suggest a "[a] method of detecting two or more target analytes in a sample" where the method comprises "providing a channel having affixed therein a two or more binding partners each specific for one for each of said two or more analytes".

Of claims 15-46, only claims 22, 26, 35, and 43, and these claims recite, respectively:

separating the mixture in an electrophoretic separation channel, [emphasis added] (claim 22)

* * *

electrophoretically separating said sets of labeled fragments in a single channel or lane, [emphasis added] (claim 26)

* * *

electrophoretically separating the mixture in a gel-filled capillary or channel, [emphasis added] (claim 35)

* * *

electrophoretically separating the mixture in a capillary or channel . . . [emphasis added] (claim 35)

The claims thus, at most, disclose capillary electrophoresis methods and devices. Capillary electrophoresis typically achieves separation of analytes by differences in analyte mobility through a "retardent" (*i.e.* a gel), and indeed such a limitation is expressly present in claim 35. The claims offer no teaching or suggestion of **a channel having affixed therein a two or more binding partners.**

Accordingly, U.S. Patent 6,361,671 fails to teach or suggest the presently claimed invention and the obviousness-type double patenting rejection of claims 1-18 in light of U.S. Patent 6,361,671 should be withdrawn.

Should the Examiner wish to maintain this rejection, Applicants request that she specifically identify a teaching or suggestion of **all of the elements of claim 1** in the claim of the 6,361,671 patent.. In particular, Applicants request that she identify with particularity a teaching or suggestion of **two or more binding partners each specific for one of said two or more analytes**, where the binding partners for each of said two or more analytes are **affixed** to a channel and **located in different regions of that channel.**

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,


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